REMARKS

The claims are rejected under 35 USC § 103(a) as being obvious over Petre *et al.* (WO 93/24148) in view of Arminjon *et al.* (AU 708777 or WO 96/37222). For the following reasons, the applicants respectfully traverse.

The present claims are drawn to a method for preparing a stabilized multi-component vaccine, the method comprising mixing at least:

a) pertussis toxoid and filamentous hemagglutinin in purified form,

b) tetanus toxoid,

c) diphtheria toxoid,

d) inactivated polio virus,

e) a conjugate of a carrier molecule selected from tetanus toxoid and diphtheria toxoid and a capsular polysaccharide of *Haemophilus influenzae* type B, and

f) an aluminum salt,

wherein tetanus toxoid and diphtheria toxoid are adsorbed onto the aluminum salt before being mixed with the other components and the conjugate is prepared in a phosphate buffer solution before being mixed with the other components. Also presented are claims to compositions made according to the method and methods of using the compositions.

The Office Action alleged that Petre *et al.* taught adsorption of tetanus and diphtheria toxoids onto aluminum salt prior to being mixed with other components, referring to Example 2 of Petre *et al.* The applicants respectfully submit that this allegation overstates the teaching. Example 2 of Petre *et al.* discloses the making of a diphtheria-tetanus-hepatitis B vaccine by combining diphtheria toxoid and tetanus toxoid adsorbed on an aluminum salt with Hepatitis B surface antigen adsorbed on aluminum phosphate. However, Petre *et al.* provides no teachings suggesting that adsorbing diphtheria toxoid and tetanus toxoid on an aluminum salt before admixing with other antigens in a multivalent vaccine is universally desirable. Faced with the task of making a multivalent comprising (as presently claimed):

a) tetanus toxoid,

b) diphtheria toxoid,

c) pertussis toxoid,

d) filamentous hemagglutinin,

e) inactivated polio virus, and

f) a conjugate of a carrier molecule selected from tetanus toxoid and diphtheria toxoid and a capsular polysaccharide of *Haemophilus influenzae* type B,

there is nothing in Petre *et al.* that suggests to the ordinary artisan that among the many combinations of two or more of the foregoing antigens, the tetanus and diphtheria components should be selected for adsorption on an aluminum salt before being admixed with the other components. In other words, it is only with the benefit of hindsight that the Examiner was able to identify Example 2 of Petre *et al.* for its disclosure of adsorbing tetanus and diphtheria toxoids onto aluminum before admixing with Hepatitis B vaccine. There is nothing in Petre *et al.* itself that distinguishes this Example for universal application to, for example, multivalent vaccines like those being claimed. On simply cannot pick and choose limitations from the prior art without some reason in the art itself to do so.

The Office Action agreed that Armijon fails to provide such a teaching or suggestion.

The Office Action admitted that Petre *et al.* does not disclose preparing the conjugate in a phosphate buffer solution before mixing it with the other components, but it alleged that one of ordinary skill in the art would have known how to prepare HiB conjugate in phosphate buffer. However, whether the ordinary artisan would know how to prepare an HiB conjugate in a phosphate buffer is irrelevant to the Patent Office's burden of establishing that the prior art suggests preparing an HiB conjugate in a phosphate buffer before admixing it with the other components. The Office Action simply fails to point to any teachings in the cited art that suggest preparing an HiB conjugate in a phosphate buffer before admixing it with the other recited components. Indeed, the Office Action expressly states that Petre *et al.* has no such teachings.

The Office Action also admitted that Arminjon *et al.* makes no such teaching or suggestion.

Moreover, not only does the cited art fail to teach or suggest a method employing either

a) adsorbing tetanus and diphtheria toxoids on an aluminum salt before mixing with pertussis toxoid, filamentous hemagglutinin, inactivated polio virus, and a conjugate of a carrier mole-cule selected from tetanus toxoid and diphtheria toxoid and a capsular polysaccharide of *Haemophilus influenzae* type B, or

b) preparing the conjugate in a phosphate buffer solution before mixing it with the other components,

the cited art fails to teach or suggest a method employing both.

A problem addressed by the presently claimed invention is the instability of the HiB valence. Petre *et al.* circumvents the instability of the HiB valence by extemporaneous addition of it to the vaccine just prior to vaccine administration, specifically stating that the HiB antigen is "used extemporaneously by formulating the vaccine just prior to administration." *See* page 4, lines 18-19. Neither Petre *et al.* nor Arminjon provides any teaching or suggestion to modify the method disclosed therein to stabilize the HiB antigen as presently claimed. Thus, it is completely unexpected that the presently claimed method would stabilize the HiB antigen.

In brief, the present claims recite methods and compositions involving a particular set of several components mixed together in a specified way. The applicants respectfully submit that the cited art neither teaches nor suggests combining all of the recited components together in a single vaccine in the manner described in the claims.

Lastly, the Applicants note that the Office Action has failed to address all the limitations in all of the claims. Each of the dependent claims contains additional limitations that further distinguish those claims from the cited art. The only additional claim limitations to which the present Office Action refers are those relating to particular amounts of components. No mention is made, however, of limitations in other claims, however. For example, claim 23 contains the limitation that the inactivated polio virus is mixed with the other components without being adsorbed onto an aluminum salt. This limitation, not taught or suggested in the cited art, has not been addressed in the Office Action.

In view of the foregoing, therefore, the present claims cannot be obvious. The Applicants respectfully request reconsideration and withdrawal of this rejection.

If there are any questions or comments regarding this Response or application, the Examiner is encouraged to contact the undersigned attorney as indicated below.

Respectfully submitted,

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